ARGUMENTS/REMARKS

Claims 1, 2, 4-6, 16-19, and 21-65 are pending. Claims 1, 4-6, 16-19, 21-22 have been amended; and claims 3, 7-15, and 20 have been cancelled, without prejudice in order to facilitate prosecution. Applicants maintain the right to pursue the previous claimed subject matter in a continuation application. Claims 23-65 are new.

Support for amended claim 1, and new claims 34, 40, and 45, appears, for example, on page 4, lines 6-12 and page 5, lines 21-29. Support for amended claims 21-22, and new claims 50, 53, 56, 59, 62, and 64 appears, for example, on page 5, lines 14-20, page 5, line 30 – page 6, line 10, and throughout the examples.

The application discloses that, among other things, peptides that have small repeating monomeric units of 2, 3, or 4 amino acid residues exhibit antimicrobial properties, and thus are useful for, among other things, a variety of industrial applications.

Priority

The Examiner has indicated that correction of the priority claim is required. The Applicants claimed priority to a prior provisional application, filed on February 24, 2003, and inadvertently made a typographical error in the Application Number. The specification has been amended to correct the typographical error.

Oath/Declaration

The Examiner has indicated that a new Declaration in compliance with 37 CFR 1.67(a) identifying the application by application number and filing date is required. A corrected Declaration is included with this response.

Specification

The Examiner has objected to the specification due to the failure to disclose the appropriate sequence identifier for the sequence for D2A21 and D4E1. A substitute sequence listing as provided for in 37 CFR § 1.825 is enclosed herein, along with the appropriate required statements. The Applicants respectfully request that the substitute sequence listing as provided be herewith entered.

Claim Rejection – 35 USC § 112, second paragraph

Claims 1-22 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite. In particular, the Examiner has stated claims 1, 10, 15, and 20 are unclear as to what the antimicrobial peptide activity of IC50 of ≤125 ug/ml is intended to act upon.

Claim 1 has been amended. Claims 10, 15, and 20 have been cancelled. Amended claim 1 is directed to an antimicrobial peptide with repeating identical monomer units of 3 or 4 residues, wherein the antimicrobial peptide has a minimum length of 14 residues, and wherein the repeating identical monomer units are selected from the group consisting of PPPN, PPNP, PNPP, NPPP, PNNN, NPNN, NNPN, NNNP, NPN, PNN, and NNP, where P is a cationic residue selected from the group consisting of lysine, ornathine, and arginine residues, wherein P is the same or a different residue within the monomer, and N is a hydrophobic residue selected from the group consisting of alanine, phenylalanine, glycine, leucine, isoleucine, threonine, tyrosine, tryptophan, valine, and methionine residues, wherein N is the same or a different residue within the monomer.

Claim 5 has been amended, and is directed to the antimicrobial peptide of claim 1, wherein the antimicrobial peptide has biocidal activity of ≤ 125 ppm for 3.5 log kill at 24 hours in a high throughput microanalysis and rapid quantitation assay against a microbe selected from the group consisting of bacteria, yeast, and fungi. Thus, as amended, claim 5 clearly recites the microbes upon which the peptide acts. Claim 6 as amended recites an antimicrobial peptide of claim 1, wherein the antimicrobial peptide has antiviral activity of ≤ 125 ppm for 3.5 log kill at 24 hr in a reverse transcriptase activity assay against a virus, and thus is definite. New claim 31 is directed to the antimicrobial peptide of claim 1, wherein the antimicrobial peptide has an IC50 of ≤ 125 μg/ml in a broth micro-dilution assay against a microbe selected from the group consisting of bacteria, yeast, and fungi. Support for claims 5-6 and 31 can be found at page 5, lines 14-20, page 7, lines 2-7, and page 10, line 17-page 11, line 2.

The amended claims are definite in accordance with 35 U.S.C. § 112, second paragraph.

Claim Rejection – 35 USC § 112, first paragraph

Enablement

The Examiner has also rejected claims 1-15 and 20 under 35 U.S.C. § 112, first paragraph, as failing to comply with the enablement requirement. Claim 1 has been amended. Claims 10, 15, and 20 have been cancelled in order to promote prosecution.

Amended claim 1 is directed to antimicrobial peptides comprising specific repeating monomeric peptide units of 3 or 4 residues, wherein the peptide has at least 14 residues. The P residue is a cationic residue selected from the group consisting of lysine, ornathine, and arginine residues, and the N is a hydrophobic residue selected from the group consisting of alanine, phenylalanine, glycine, leucine, isoleucine, threonine, tyrosine, tryptophan, valine, and methionine residues.

The amended claims are fully enabled. The specification provides sufficient disclosure for one of skill in the art to make and use the claimed subject matter. The specification provides a large number of exemplary periodic antimicrobial peptides, and describes the antimicrobial activities of such peptides based on IC50, MIC, and TX50 values, and describes the protocols utilized to determine these values.

The specification clearly enables the scope of the peptides recited in the claims. The specification provides methods for selecting and testing the peptides. In particular, the application discloses for example on page 5, paragraph 23, and Table 1, what the peptides are. The application teaches on pages 5-6, paragraph 24, and in Examples 2 and 3, for example, how to use the peptides in inhibiting microbial growth. The application further discloses how to determine antimicrobial activity of peptides, e.g., how to determine IC50's for a target microbe. See, e.g., Examples 2 and 3 of the present application. The determination of an IC50 is a well known technique known in the art. Furthermore, the specification provides detailed examples of specific periodic peptide sequences.

A skilled person in the art, with the guidance provided for in the specification (and in particular, the exemplary peptides) and the general knowledge of the field (including the knowledge in the field regarding the production of synthetic and recombinant peptides) would be able to make and use the peptides recited in the claims.

On page 4, line 13-14, the specification discloses that monomers may be produced synthetically, or through microbial, viral, or enzymatic expression. These techniques are well-known and routinely utilized in the art. In the background of the specification, the Applicants cite a number of examples of methods utilized to produce periodic peptides, including the synthetic manufacture as practiced by Demegen, Inc., the synthetic production of D2A21, and the polymerization techniques as described in US Pat. No. 5,789,542 to McLauglin, and Javadpour, et al., "Efficacy of a synthetic lytic peptide in the treatment of prostate cancer," Urol. Oncol. (2001) 6(3): 97-102. In addition, synthetic production of peptides has been common in the art for a number of years, both through solution phase and solid phase synthesis. Numerous scientific articles, books, and reviews exist describing peptide production.

The Examiner noted that the periodic antimicrobial peptides were ordered from a known manufacturer (citing page 6, paragraph 25). It is noted that the Applicants obtained these compounds from a custom manufacturer. The peptides were custom made at Applicants request, and were not otherwise commercially available. The presently amended claims are fully enabled based on the detailed disclosure in the specification and knowledge available in the art.

Written Description

The Examiner has also rejected claims 1-15 and 20 under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement.

Claim 1 has been amended, and claims 10-15 and 20 have been cancelled. Applicant submits that the amended claims fully comply with the written description of 35 U.S.C. § 112, first paragraph. See Tables 1-6 of the present application and the provided exemplary antimicrobial peptides in the specification, which are indicative of actual reduction to practice of particular embodiments that meet all of the limitations of the claim. *See, e.g., Cooper v. Goldfarb*, 154 F.3d 1321 (Fed. Cir. 1998).

The claimed subject matter is fully described in the specification. The claims recite antimicrobial periodic peptides with repeating identical monomeric units of 2, 3, or 4 residues, with formulas for the monomeric peptides, such as NNNP or PNNN, made up of a defined group of cationic residues and a defined group of hydrophobic residues sufficient enough to show

possession. The specification further provides numerous exemplary peptides and their antimicrobial activity.

The specification provides sufficient disclosure for one of skill in the art to make and use the peptide recited in the claims. The specification provides a large number of exemplary periodic antimicrobial peptides, and describes the antimicrobial activities of such peptides based on IC50, MIC, and TX50 values, and describes the protocols utilized to determine these values. The application for example on page 5, paragraph 23, and Table 1, provides a detailed description of the peptides. The application for example on pages 5-6, paragraph 24, and in Examples 2 and 3, discloses how to use the peptides in inhibiting microbial growth. The application further discloses how to determine antimicrobial activity of peptides. See, e.g., Examples 2 and 3 of the present application. Furthermore, the specification provides detailed examples of specific periodic peptide sequences. Thus, the claimed subject matter is clearly described in accordance with U.S.C. § 112, first paragraph.

Claim Rejection – 35 USC § 102(b)

The Examiner has also rejected claims 1-18 under 35 USC § 102(b) as being anticipated by U.S. Pat. No. 5,856,435 to Bazile et al. Bazile et al. discloses the general formula (LKKL)n and (LKLK)n, wherein n is defined as being an integer greater than four. Bazile et al. teaches the use of such peptides for use in the transfer of nucleic acids into eukaryotic cells.

The Examiner likewise rejected claims 1-18 under 35 USC § 102(b) as being anticipated by Seipke et al. (1980) International Journal of Biological Macromolecules, 2(4): 268-270. Seipke et al. disclose the formula (KFK)n, wherein n is defined as being an integer equal to 3-9.

"A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631 (Fed. Cir. 1987). Applicants respectfully draw the attention of the Examiner to presently amended claims. The applied art of Bazile et al. and Seipke et al. does not identically disclose the subject matter of the amended claims. Claims 1, 2, 4-6, 16-19, and 31-49 as amended do not recite a peptide of the general formula (LKKL)n or (LKLK)n, or a peptide of the formula (KFK)n, where n is equal to 3-9.

Claims 21-30, and 50-65 are directed to a process of inhibiting growth or killing of a target cell which is not disclosed in Bazile et al. or Seipke et al., cited by the Examiner.

Accordingly, the Applicants respectfully request that the rejection under 35 U.S.C. § 102(b) be withdrawn.

Conclusion

The Commissioner is authorized to charge such fees due with this response above those submitted, or credit any overpayment to Deposit Account No. 11-0980.

Applicant respectfully requests that a timely Notice of Allowance be issued in this case.

Respectfully submitted,

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